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EXAMINER

LU, FRANK WEI MIN

ART UNIT	PAPER NUMBER
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1634

DATE MAILED: 09/16/2002

16

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/829,066

Applicant(s)

NISSON ET AL.

Examiner

Frank W Lu

Art Unit

1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 July 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4 and 6-71 is/are pending in the application.
- 4a) Of the above claim(s) 9-40 and 42-71 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4, 6-8 and 41 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5 and 15. 6) ☐ Other:

Art Unit: 1634

DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of Group I, claims 1-4, 6-8, and 41 and species of cDNA library and circular DNA in Paper No. 14 is acknowledged. The traversal is on the ground(s) that: (1) there is no serious burden on the examiner since "Groups I-III are closely related in subject matter." ; (2) "groups I and II have been classified by the Examiner in class 436, subclass 94."; (3) "[T]he three groups of species identified by the Examiner in paragraphs 5, 6, 7 of the Restriction Requirement respectfully contain members that are closely related in subject matter. As such, a search of one of these alleged species is likely to encompass subject matter pertinent to the patentability of all members, particularly since the points of novelty of each member lies primarily in one of claims 1, 9 or 42 from which it depends."

After carefully considered applicant's arguments, the examiner agreed to withdraw the species election that "lies primarily in one of claims 1, 9 or 42 from which it depends" (see page 5 of previous office action). However, these arguments have not been found persuasive toward the withdrawal of the restriction requirement and other species elections nor persuasive toward the relaxation of same such that Groups I to III will be examined together. First, Groups I-III are not closely related in subject matter and they are methods which comprise different method steps. As stated in previous office action, since Group II such as one or more haptenylated probes in step (a) of claim 9 is not required for Group I, the search required for Group III such as step (c) of claim 42 is not required for Groups I and II, there is a search burden on the examiner. Second, "groups I and II have been classified by the Examiner in class 436, subclass 94." is not the reason

Art Unit: 1634

for the restriction. Third, although species identified by the Examiner in paragraphs 6 and 7 of the Restriction Requirement are related, they are directed to different products and will require different searches. For example, comparing with linear single stranded DNA, circular single stranded DNA has different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01) such as using in rolling circle amplification.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-4, 6-8, and 41 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. .

Although the specification describes that different amino acid and imidazole can be used as a denaturant of double stranded nucleic acid (for example, see specification, page 16), the specification does not adequately describe that said denaturant is not selected from the group consisting of asparagine and β -alanine as recited in claims 1-4, 6-8, and 41. MPEP 2163.06 states that "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." In view of the embodiments adequately description in the

Art Unit: 1634

specification, the subject application does not reasonably convey to one skilled in the art that applicant was in possession of the full scopes of products encompass in the claims at the time of the application was filled. Therefore, the written description requirement has not been satisfied.

In support of this position, attention is directed to the decision of *Vas-Cath inc. V.*

Mahurkar 19 USPQ2d 1111 (CAFC, 1991):

This court in *Wilder* (and the CCPA before it) clearly recognized, and we hereby reaffirm, that 35 U.S.C. 112, first paragraph, requires a "written description of the invention" which is separate and distinct from the enablement requirement. The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the "applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed*.

4. Claims 1-4, 6-8, and 41 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using certain amino acid at certain experimental condition as a denaturant to dissociate a double stranded DNA, does not reasonably provide enablement for: (1) using any kind of amino acid at any kind of experimental condition as a denaturant to dissociate a double stranded DNA; and (2) using any kind of polyamino acids as a denaturant to dissociate a double stranded DNA. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. .

In *In re Wands*, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court considered the issue of enablement in molecular biology. The Court summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the

Art Unit: 1634

presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims. The Court also stated that although the level of skill in molecular biology is high, results of experiments in molecular biology are unpredictable.

To begin, there is no direction or guidance in the specification that any kind of amino acid at any kind of experimental condition and any kind of polyamino acids can serve as a denaturant to dissociate a double stranded DNA. While the relative skill in the art is very high (the Ph.D. degree with laboratory experience), there is no predictability whether any kind of amino acid at any kind of experiment condition and any kind of polyamino acids can serve as a denaturant to dissociate a double stranded DNA.

Claims 1-4, 6-8 and 41 are directly to a method for denaturing or separating double-stranded nucleic acid molecules. An amino acid denaturant in claim 1 was read as any kind of compound with amino group and carboxyl group and polyamino acids in claim 2 was read as any kind of peptide or polypeptide or protein. The specification only describes that common amino acids, imidazole, and polyamino acid can be used to dissociate or denature a double-stranded nucleic acid molecule (for example, see page 16). However, there is no experimental data in the specification to show how these common amino acids, imidazole, and polyamino acid work as a denaturant to dissociate a double stranded nucleic acid molecule. Furthermore, the specification does not provide a guidance to show that any kind of amino acid at any kind of experimental condition and any kind of polyamino acids can serve as a denaturant to dissociate a double stranded DNA. In fact, during prior art search (including applicant's papers), the examiner found

Art Unit: 1634

that at least two references supported the examiner's position. Chadalavada *et al.*, (FEBS Letters, 410, 201-205, June 1997) showed that 2 M glycine, 2 M serine, 1 M alanine, 0,25 M valine, 0.1 M leucine was no effect on T_m of calf thymus DNA (see page 202, Table 1) and suggested that these common amino acids could not be served as a denaturant of double stranded DNA at least in their experimental conditions. Liquier *et al.*, (Biochemistry, 14, 4191-4197, 1975) showed that poly(L-lysine) increased T_m of double stranded DNA and suggested that poly(L-lysine) was no effect on the conformational flexibility of DNA (see abstract in page 4191). Therefore, only certain amino acid at certain experimental condition can serve as a denaturant to dissociate a double stranded DNA. Accordingly, it is concluded that undue experimentation is required to make the invention as it is claimed. These undue experimentation at least includes to test whether any kind of amino acid at any kind of experiment conditions and any kind of polyamino acids can serve as a denaturant of double stranded DNA.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Art Unit: 1634

6. Claims 1, 2, and 41 are rejected under 35 U.S.C. 102(b) as being anticipated by Rees *et al.*, (Biochemistry, 32, 137-144, 1993) as evidence by Freifelder (Physical Biochemistry: Applications to Biochemistry and Molecular Biology, second edition, pages 508-510, 1982).

Rees *et al.*, teach the effect of betaine (N, N, N-trimethylglycine) on the melting behavior of calf thymus DNA. Figure 1 showed that 5 M of betaine greatly sharpened the melting transition and shifts it to a lower temperature (see left column in page 138 and right column in page 139).

Freifelde teach melting curve during the helix-coil transition of double-stranded DNA. Since it was known that double strand separation did not occur until well past the optical-transition region in a melting curve during the process of double-stranded DNA denaturation (see Freifelder, pages 508 and 509), the plateau region of curves 1 and 2 (a region past transition region) in Figure 1A indicated that double stranded DNA was separated to form a single stranded DNA after temperature was reached to certain degree (see Figure 1A). Note that: (1) betaine was considered as an unnatural amino acid as recited in claims 1, 2, and 41 since its chemical name was N, N, N-trimethylglycine; and (2) betaine was considered as an amino acid denaturant as recited in claims 1 and 2 since it eliminated different stability between AT-rich region and GC-rich region in random-sequence DNA (AT-rich region and GC-rich region had different melting behaviors), shifted the melting temperatures of DNAs of all base pair compositions to a single value, and finally formed a single stranded DNA (see left column in page 138, right column in page 139, and Figure 1A).

Art Unit: 1634

Therefore, Rees *et al.*, as evidence by Freifelder teach all limitations recited in claims 1, 2, and 41.

7. Claims 1, 2, 4, 6-8, and 41 are rejected under 35 U.S.C. 102(b) as being anticipated by Aslanyan *et al.*, (Biophysics, 29, 615-620, 1984).

Aslanyan *et al.*, teach the effect of glycine on conformation and thermal stability of DNA. As shown in Figures 1 and 2, glycine concentration with range of 1 mM- 3000 mM (log10=1000 mM, see Figure 1) as recited in claims 6-8 was shown to reduce the melting point of calf thymus DNA. The intermolecular interaction between DNA and glycine caused sharp fall in the enthalpy of the helix-coil transition and led to uncoiling of the DNA double helix (causing double stranded DNA to become single stranded) (see abstract in page 615, pages 616 and 617, and Figures 1 and 2). Glycine was considered as a natural amino acid denaturant as recited in claim 4 and 41.

Therefore, Aslanyan *et al.*, teach all limitations in claims 1, 2, 4, 6-8, and 41.

Double Patenting

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686

Art Unit: 1634

F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 1-4, 6-8, and 41 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9 of U.S. Patent No.6,268,133. Although the conflicting claims are not identical, they are not patentably distinct from each other because the examined claims in this instant application is either anticipated by, or would have been obvious over, the reference claims. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969). Note that, although claims 1-4, 6-8 and 41 in this instant application are not identical to claims 1-9 and are more broader than claims 1-9 of U.S. Patent No.6,268,133, claims 1-9 of U.S. Patent No.6,268,133 are directed to the same subject matter and fall entirely

Art Unit: 1634

within the scope of claims 1-4, 6-8, and 41 in this instant application. In other words, claims 1-4, 6-8, and 41 in this instant application are anticipated by claims 1-9 of U.S. Patent No. 6,268,133.

Conclusion

10. No claim is allowed.


11. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (703) 308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (703) 305-1270. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application should be directed to the patent Analyst of the Art Unit, Ms. Chantae Dessau, whose telephone number is (703) 605-1237.

Frank Lu
September 4, 2002


ETHAN C. WHISENANT
PRIMARY EXAMINER